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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,701	01/05/2001	Allan S. Hoffman	UWOTL119001	3998

26389 7590 06/27/2005

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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/755,701	HOFFMAN ET AL.	
	Examiner	Art Unit	
	MY-CHAU T. TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,8,9,13-17,19,33-36 and 38-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *38-44* is/are allowed.

6)☒ Claim(s) *2-4,8,9,13-17,19 and 33-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/25/2005 has been entered.

Application and Claims Status

2. Applicant's amendment and response filed 02/08/2005 is acknowledged and entered. Claims 6, 18, and 20-32 have been cancelled. Claims 2-4, 8, 13, 17, 19, 33, and 34 have been amended. Claims 38-44 have been added.

3. Claims 11 and 37 were cancelled and Claims 3, 8, and 13 were amended by the amendment filed on 02/18/2004.

4. Claims 1, 5, 7, and 12 were cancelled; Claims 2-4, 6, 8-11, and 13-19 were amended; and Claims 33-37 were added by the amendment filed on 06/24/2003.

5. Claims 2-4, 8, 9, 13-17, 19, 33-36, and 38-44 are pending.

Election/Restrictions

6. Applicant has elected with traverse the following species for the elected invention (Claims 2-4, 8, 9, 13-17, 19, 33-36, and 38-44) in the reply filed on 5/10/2004 and 8/16/2004:

a. A ***single specific*** species of hydrophobic component. Applicant has elected the terpolymer of dimethylaminoethyl methacrylate (DMAEMA), butyl methacrylate (BMA), and styrene benzaldehyde, which is described in Example 2 and illustrated in Figures 4 and 5.

b. A ***single specific*** species of hydrophilic component. Applicant has elected polyalkylene oxide (e.g., PEG).

c. A ***single specific*** species of pH-sensitive linkage. Applicant has elected acetal.

7. Claim 18 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***nonelected species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/10/2004 and 8/16/2004. However, claim 8 is cancelled by the amendment filed 02/28/2005.

8. Claims 2-4, 8, 9, 13-17, 19, 33-36, and 38-44 are treated on the merit in this Office Action.

Priority

9. The instant application is granted the benefit of priority for the provisional application 60/174,893 filed 01/07/2000 under 35 U.S.C 119(e).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 2-4, 8-10, 13-15, 19, and 33-35 rejected under 35 U.S.C. 102(e) as being anticipated by Choi et al. (US Patent 6,210,717 B1).

Choi et al. discloses a composition for delivering a selected nucleic acid and various kinds of ligands into a targeted host cell (see e.g. Abstract; col. 2, lines 29-55; col. 3, lines 12-34; col. 3, lines 54-63). The composition is a copolymer transport molecule that is comprised of a hydrophilic portion, a hydrophobic portion, and a functional moiety (refers to the claimed agent) coupled to the hydrophilic portion (see e.g. col. 2, lines 29-55; col. 3, lines 12-26; col. 4, lines 60-62). The hydrophilic portion and hydrophobic portion are linked through as amide bond or a graft copolymer comprising a hydrophobic polyester portion and a hydrophilic cation portion wherein the hydrophilic cation include polymer such as poly(L-serine ester) and poly(D-serine ester) (refers to the claimed pH-sensitive linkage)(see e.g. col. 2, lines 29-55; col. 6, lines 45-57). The functional moiety includes ligand, and nucleic acid (see e.g. col. 3, lines 12-26). Thus the composition of Choi et al. anticipates the presently claimed composition.

Additionally, the limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is a functional

limitation or a property of the claimed pH-sensitive linkage and it is presumed to be inherent. See MPEP § 2112.01. MPEP § 2112.01 states that:

> *II. >< COMPOSITION CLAIMS — IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES*
>
> *"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").*

The polymer linkage of Choi et al. is the same as the claimed pH-sensitive linkage of claim 8, i.e. an ester bond. Thus, the claimed functional limitation of the pH-sensitive linkage is inherent to the peptide linkage Choi et al. The limitation that the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane are a functional limitation or a property of the claimed hydrophobic conjugate and it is presumed to be inherent since the copolymer of Choi et al. is the same as the claimed hydrophobic component of claims 4 and 35.

12. Claims 2-4, 8-10, 13-15, 19, and 33-35 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Choi et al. (US Patent 6,210,717 B1).

Choi et al. discloses a composition for delivering a selected nucleic acid and various kinds of ligands into a targeted host cell (see e.g. Abstract; col. 2, lines 29-55; col. 3, lines 12-34; col. 3, lines 54-63). The composition is a copolymer transport molecule that is comprised of a hydrophilic portion, a hydrophobic portion, and a functional moiety (refers to the claimed agent) coupled to the hydrophilic portion (see e.g. col. 2, lines 29-55; col. 3, lines 12-26; col. 4, lines

60-62). The hydrophilic portion and hydrophobic portion are linked through as amide bond or a graft copolymer comprising a hydrophobic polyester portion and a hydrophilic cation portion wherein the hydrophilic cation include polymer such as poly(L-serine ester) and poly(D-serine ester) (refers to the claimed pH-sensitive linkage) (see e.g. col. 2, lines 29-55). The functional moiety includes ligand, and nucleic acid (see e.g. col. 3, lines 12-26). Thus the composition of Choi et al. anticipates the presently claimed composition.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitations of a) "*the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component*", i.e. the functional limitation of the pH-sensitive linkage, and b) "*the hydrophobic component is membrane-disruptive and allows enhanced transport through a membrane only when released from the hydrophilic conjugate*", i.e. the functional limitation of the hydrophobic component. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the composition of Choi et al. are the same as the structural features of the claimed composition, which are a hydrophobic component and a hydrophilic component that are linked by a pH-sensitive linkage. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference pH-sensitive linkage and hydrophobic component wherein the ability of the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component and the ability of the hydrophobic component to be membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate. In the absence

of evidence to the contrary, the burden is upon the applicant to prove that the claimed composition is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

13. Claims 2-4, 8-10, 13-16, 19, and 33-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Heller et al. (US Patent 5,939,453).

Heller et al. discloses a composition that is block copolymers having both hydrophilic and hydrophobic blocks (see e.g. Abstract; col. 4, lines 1-11; col. 5, lines 10-17). This composition provides a pharmaceutical delivery system or for the sustained release of an active agent wherein the active agent include proteins and enzymes (see e.g. col. 4, lines 1-11, and 25-67). The hydrophilic block is PEG (polyethylene glycol) and the hydrophobic block is POE (poly(orthoester)), which is bioerodible (see e.g. col. 5, lines 10-17; col. 6, lines 7-35). The hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The composition includes a pharmaceutical carrier (see e.g. col. 5, lines 58-67; col. 13, lines 47-60). Thus the composition of Heller et al. anticipates the presently claimed composition.

Additionally, the limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is a functional limitation or a property of the claimed pH-sensitive linkage and it is presumed to be inherent. See MPEP § 2112.01. MPEP § 2112.01 states that:

II. >< COMPOSITION CLAIMS — IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES

> *"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").*

The acetal linkage of Heller et al. is the same as the claimed pH-sensitive linkage of claim 8, i.e. acetal. Thus, the claimed functional limitation of the pH-sensitive linkage is inherent to the peptide linkage Heller et al. The limitation that the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane are a functional limitation or a property of the claimed hydrophobic conjugate and it is presumed to be inherent since the copolymer of Heller et al. is the same as the claimed hydrophobic component of claims 4 and 35.

14. Claims 2-4, 8-10, 13-16, 19, and 33-36 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Heller et al. (US Patent 5,939,453).

Heller et al. discloses a composition that is block copolymers having both hydrophilic and hydrophobic blocks (see e.g. Abstract; col. 4, lines 1-11; col. 5, lines 10-17). This composition provides a pharmaceutical delivery system or for the sustained release of an active agent wherein the active agent include proteins and enzymes (see e.g. col. 4, lines 1-11, and 25-67). The hydrophilic block is PEG (polyethylene glycol) and the hydrophobic block is POE (poly(orthoester)), which is bioerodible (see e.g. col. 5, lines 10-17; col. 6, lines 7-35). The

hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The composition includes a pharmaceutical carrier (see e.g. col. 5, lines 58-67; col. 13, lines 47-60). Thus the composition of Heller et al. anticipates the presently claimed composition.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitations of a) "*the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component*", i.e. the functional limitation of the pH-sensitive linkage, and b) "*the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate*", i.e. the functional limitation of the hydrophobic component. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the composition of Heller et al. are the same as the structural features of the claimed composition, which are a hydrophobic component and a hydrophilic component that are linked by a pH-sensitive linkage. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference pH-sensitive linkage and hydrophobic component wherein the ability of the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component and the ability of the hydrophobic component to be membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed array is different from the one taught by prior art and to establish the patentable differences. See *In re*

Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Withdrawn Rejection(s)

15. The rejections of claims 2-4, 6, 8, 13, 16-17, and 19 under 35 USC 112, second paragraph, as being indefinite have been withdrawn in light of applicant's amendments of claims 2-4, 8, 13, 17, 19, 33, and 34.

16. The rejection of claims 2-4, 8-10, 14-15, and 33-35 under 35 USC 102(b) as being anticipated by Kopecek et al. (US Patent 5,258,453) has been withdrawn in light of applicant's amendments of claim 8 wherein the species of amide bond for the claimed type of pH-sensitive linkage was deleted.

17. The rejection of claims 2-4, 8-10, 14-15, and 33-35 under 35 USC 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Kopecek et al. (US Patent 5,258,453) has been withdrawn in light of applicant's amendments of claim 8 wherein the species of amide bond for the claimed type of pH-sensitive linkage was deleted.

Response to Arguments

18. Applicant's argument directed to the rejection under 35 USC 102(e) as being anticipated by Choi et al. (US Patent 6,210,717 B1) for claims 2-4, 8-10, 13-15, 19, and 33-35 was considered but they are not persuasive for the following reasons.

Choi et al. discloses a composition for delivering a selected nucleic acid and various kinds of ligands into a targeted host cell (see e.g. Abstract; col. 2, lines 29-55; col. 3, lines 12-34; col. 3, lines 54-63). The composition is a copolymer transport molecule that is comprised of a hydrophilic portion, a hydrophobic portion, and a functional moiety (refers to the claimed agent) coupled to the hydrophilic portion (see e.g. col. 2, lines 29-55; col. 3, lines 12-26; col. 4, lines 60-62). The hydrophilic portion and hydrophobic portion are linked through as amide bond or a graft copolymer comprising a hydrophobic polyester portion and a hydrophilic cation portion wherein the hydrophilic cation include polymer such as poly(L-serine ester) and poly(D-serine ester) (refers to the claimed pH-sensitive linkage) (see e.g. col. 2, lines 29-55). The functional moiety includes ligand, and nucleic acid (see e.g. col. 3, lines 12-26). Thus the composition of Choi et al. anticipates the presently claimed composition.

Additionally, the limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is a functional limitation or a property of the claimed pH-sensitive linkage and it is presumed to be inherent. See MPEP § 2112.01. MPEP § 2112.01 states that:

> *II. >< COMPOSITION CLAIMS — IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES*
> *"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").*

The polymer linkage of Choi et al. is the same as the claimed pH-sensitive linkage of claim 8, i.e. an ester bond. Thus, the claimed functional limitation of the pH-sensitive linkage is inherent to the peptide linkage Choi et al. The limitation that the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane are a functional limitation or a property of the claimed hydrophobic conjugate and it is presumed to be inherent since the copolymer of Choi et al. is the same as the claimed hydrophobic component of claims 4 and 35.

Applicant alleges that the composition of Choi et al. does not anticipate the presently claimed invention because the reference of Choi et al. does not teach or suggest a pH-sensitive linkage. Thus, the composition of Choi et al. does not anticipate the presently claimed invention.

Applicant's arguments are not convincing since the composition of Choi et al. does anticipate the presently claimed invention because the reference of Choi et al. does teach or suggests a pH-sensitive linkage. Choi et al. disclose a graft copolymer comprising a hydrophobic polyester portion and a hydrophilic cation portion wherein the hydrophilic cation include polymer such as poly(L-serine ester) and poly(D-serine ester), i.e. an ester bond between the hydrophobic portion and the hydrophilic portion (col. 2, lines 40-55; col. 6, lines 45-57). The 'ester linkage' of the composition of Choi et al. is the same as the claimed pH-sensitive linkage of claim 8. Thus, the composition of Choi et al. does anticipate the presently claimed invention, and the rejection is maintained.

19. Applicant's argument directed to the rejection under 35 USC 102 (e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Choi et al. (US Patent 6,210,717 B1) for claims 2-4, 8-10, 13-15, 19, and 33-35 was considered but they are not persuasive for the following reasons.

Choi et al. discloses a composition for delivering a selected nucleic acid and various kinds of ligands into a targeted host cell (see e.g. Abstract; col. 2, lines 29-55; col. 3, lines 12-34; col. 3, lines 54-63). The composition is a copolymer transport molecule that is comprised of a hydrophilic portion, a hydrophobic portion, and a functional moiety (refers to the claimed agent) coupled to the hydrophilic portion (see e.g. col. 2, lines 29-55; col. 3, lines 12-26; col. 4, lines 60-62). The hydrophilic portion and hydrophobic portion are linked through as amide bond or a graft copolymer comprising a hydrophobic polyester portion and a hydrophilic cation portion wherein the hydrophilic cation include polymer such as poly(L-serine ester) and poly(D-serine ester) (refers to the claimed pH-sensitive linkage) (see e.g. col. 2, lines 29-55). The functional moiety includes ligand, and nucleic acid (see e.g. col. 3, lines 12-26). Thus the composition of Choi et al. anticipates the presently claimed composition.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitations of a) "*the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component*", i.e. the functional limitation of the pH-sensitive linkage, and b) "*the hydrophobic component is membrane-disruptive and allows enhanced transport through a membrane only when released from the hydrophilic conjugate*", i.e. the functional limitation of the hydrophobic component. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the composition of Choi et al. are the same as the structural features of the claimed composition, which are a hydrophobic component and a hydrophilic component that are linked by a pH-sensitive linkage. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference pH-sensitive linkage and hydrophobic component wherein the ability of the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component and the ability of the hydrophobic component to be membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed composition is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Applicant argues that he composition of Choi et al. does not anticipate or is not obvious over the presently claimed invention because the reference of Choi et al. does not teach or suggest a pH-sensitive linkage. Thus, the composition of Choi et al. does not anticipate or is obvious the presently claimed invention.

Applicant's arguments are not convincing since the composition of Choi et al. does anticipate or is obvious over the presently claimed invention because the reference of Choi et al.

does teach or suggests a pH-sensitive linkage. Choi et al. disclose a graft copolymer comprising a hydrophobic polyester portion and a hydrophilic cation portion wherein the hydrophilic cation include polymer such as poly(L-serine ester) and poly(D-serine ester), i.e. an ester bond between the hydrophobic portion and the hydrophilic portion (col. 2, lines 40-55; col. 6, lines 45-57). The 'ester linkage' of the composition of Choi et al. is the same as the claimed pH-sensitive linkage of claim 8. Additionally, applicant has not provided any evidence that the claimed composition is different from the composition of the Choi et al. Thus, the composition of Choi et al. does anticipate the presently claimed invention, and the rejection is maintained.

20. Applicant's arguments directed to the rejection under 35 USC 102(e) as being anticipated by Heller et al. (US Patent 5,939,453) for claims 2-4, 8-10, 13-16, 19, and 33-36 were considered but they are not persuasive for the following reasons.

Heller et al. discloses a composition that is block copolymers having both hydrophilic and hydrophobic blocks (see e.g. Abstract; col. 4, lines 1-11; col. 5, lines 10-17). This composition provides a pharmaceutical delivery system or for the sustained release of an active agent wherein the active agent include proteins and enzymes (see e.g. col. 4, lines 1-11, and 25-67). The hydrophilic block is PEG (polyethylene glycol) and the hydrophobic block is POE (poly(orthoester)), which is bioerodible (see e.g. col. 5, lines 10-17; col. 6, lines 7-35). The hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The composition includes a pharmaceutical carrier (see e.g. col. 5, lines 58-67; col. 13, lines 47-60). Thus the composition of Heller et al. anticipates the presently claimed composition.

Additionally, the limitation that the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component is a functional limitation or a property of the claimed pH-sensitive linkage and it is presumed to be inherent. See MPEP § 2112.01. MPEP § 2112.01 states that:

> *II. >< COMPOSITION CLAIMS — IF THE COMPOSITION IS PHYSICALLY THE SAME, IT MUST HAVE THE SAME PROPERTIES*
> *"Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990) (Applicant argued that the claimed composition was a pressure sensitive adhesive containing a tacky polymer while the product of the reference was hard and abrasion resistant. "The Board correctly found that the virtual identity of monomers and procedures sufficed to support a prima facie case of unpatentability of Spada's polymer latexes for lack of novelty.").*

The acetal linkage of Heller et al. is the same as the claimed pH-sensitive linkage of claim 8, i.e. acetal. Thus, the claimed functional limitation of the pH-sensitive linkage is inherent to the peptide linkage Heller et al. The limitation that the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane are a functional limitation or a property of the claimed hydrophobic conjugate and it is presumed to be inherent since the copolymer of Heller et al. is the same as the claimed hydrophobic component of claims 4 and 35.

Applicant contends that the composition of Heller et al. does not anticipate the presently claimed invention because 1) the reference of Heller et al. does not teach or suggest a pH-sensitive linkage, and 2) the reference of Heller et al. does not teach or suggest the release of the hydrophilic component from the hydrophilic component. Thus, the composition of Heller et al. does not anticipate the presently claimed invention.

Applicant's arguments are not convincing since the composition of Heller et al. does anticipate the presently claimed invention. First, Heller et al. does or suggests a pH-sensitive linkage. Heller et al. disclose that the hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The acetal bond is one of the claimed species of instant claim 8 and the elected species of the pH-sensitive linkage. Second, Heller et al. does or suggests the release of the hydrophilic component from the hydrophilic component. Heller et al. define the terms *"bioerodible" and "biodegradable" as referring to the degradation,* ***disassembly****, or digestion of the polymer by action of a biological environment including the action of living organisms, and most notably at physiological pH and temperature* (col. 5, lines 9-13). Thus, the composition of Heller et al. does anticipate the presently claimed invention, and the rejection is maintained.

21. Applicant's arguments directed to the rejection under 35 USC 102 (e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Heller et al. (US Patent 5,939,453) as for claims 2-4, 8-10, 13-16, 19, and 33-36 were considered but they are not persuasive for the following reasons.

Heller et al. discloses a composition that is block copolymers having both hydrophilic and hydrophobic blocks (see e.g. Abstract; col. 4, lines 1-11; col. 5, lines 10-17). This composition provides a pharmaceutical delivery system or for the sustained release of an active agent wherein the active agent include proteins and enzymes (see e.g. col. 4, lines 1-11, and 25-67). The hydrophilic block is PEG (polyethylene glycol) and the hydrophobic block is POE (poly(orthoester)), which is bioerodible (see e.g. col. 5, lines 10-17; col. 6, lines 7-35). The hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The composition includes a pharmaceutical carrier (see e.g. col. 5, lines 58-67; col. 13, lines 47-60). Thus the composition of Heller et al. anticipates the presently claimed composition.

Alternatively, the claimed invention further differs from the prior art teachings only by the recitations of a) "*the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component*", i.e. the functional limitation of the pH-sensitive linkage, and b) "*the hydrophobic component is membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate*", i.e. the functional limitation of the hydrophobic component. The claimed invention appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The structural features of the composition of Heller et al. are the same as the structural features of the claimed composition, which are a hydrophobic component and a hydrophilic component that are linked by a pH-sensitive linkage. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare the specific activities of the instant versus the reference pH-sensitive linkage and hydrophobic component wherein the ability of the pH-sensitive linkage is stable at a pH between 6.8 and 8 and hydrolyzed at a pH less than 6.5 to release the hydrophobic component and the ability of the hydrophobic component to be membrane-disruptive and allows enhanced transport through a cellular membrane only when released from the hydrophilic conjugate. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed composition is different from the one taught by prior art and to establish the patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ2d 1922(PTO Bd. Pat. App. & Int. 1989). See also MPEP 2112.01.

Applicant argues that the composition of Heller et al. does not anticipate or is not obvious over the presently claimed invention because 1) the reference of Heller et al. does not teach or suggest a pH-sensitive linkage, and 2) the reference of Heller et al. does not teach or suggest the release of the hydrophilic component from the hydrophilic component. Thus, the composition of Heller et al. does not anticipate the presently claimed invention.

Applicant's arguments are not convincing since the composition of Heller et al. does anticipate or is obvious over the presently claimed invention. First, Heller et al. does or suggests a pH-sensitive linkage. Heller et al. disclose that the hydrophilic block is linked to the hydrophobic block via an acetal bond (refers to the pH-sensitive linkage) (see e.g. col. 8, lines 24-50; col. 8, line 63 to col. 9, line 15). The acetal bond is one of the claimed species of instant claim 8 and the elected species of the pH-sensitive linkage. Second, Heller et al. does or

suggests the release of the hydrophilic component from the hydrophilic component. Heller et al. define the terms *"bioerodible" and "biodegradable" as referring to the degradation, **disassembly**, or digestion of the polymer by action of a biological environment including the action of living organisms, and most notably at physiological pH and temperature* (col. 5, lines 9-13). Third, applicant has not provided any evidence that the claimed composition is different from the composition of the Choi et al. Thus, the composition of Heller et al. does anticipate or is obvious over the presently claimed invention, and the rejection is maintained.

Allowable Subject Matter

22. The following is a statement of reasons for the indication of allowable subject matter of claims 38-44:

The cited prior arts do not teach or fairly suggest the instant claimed composition of claims 38-44 comprising the combination of a hydrophobic synthetic vinyl-type polymer, a plurality of pendant hydrophilic polyalkylene oxide, and a plurality of pH-sensitive linkages.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 571-272-0810. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
June 23, 2005

PADMASHRI PONNALURI
PRIMARY EXAMINER